

The Truth Behind Subchondral Cysts in Osteoarthritis of the Knee

Han Xinyun Audrey, Hamid Rahmatullah Bin Abd Razak* and Tan Hwee Chye Andrew

Department of Orthopaedic Surgery, Singapore General Hospital, Outram Road, 169608, Singapore

Abstract: *Background:* Subchondral cysts have always been taught to be one of the cardinal radiological features of knee osteoarthritis but are not well understood. We aimed to evaluate the radiological prevalence and epidemiology of subchondral cysts in patients with knee osteoarthritis to determine if they are truly a cardinal radiological feature.

Methods: All patients of a single surgeon with symptoms of knee osteoarthritis were selected for this study. All patients had failed a trial of conservative therapy and were planned for total knee arthroplasty. Patients with symptoms of and documentary evidence of inflammatory arthritis, other neurological and orthopaedic problems causing functional deficits were excluded from this study. A total of 806 plain radiographs were analyzed with the aid of an atlas for the presence of narrowed joint space, osteophytes, subchondral sclerosis and subchondral cysts. The radiological prevalence of each feature was then calculated. Demographics and pre-operative measurements were compared between patients with and without radiological evidence of subchondral cysts.

Results: Subchondral cysts were only present in 30.6% of the study population. Narrowed joint space was present in 99.5%, osteophytes in 98.1% and subchondral sclerosis in 88.3% of all radiographs. The differences in prevalence were statistically significant. There was a higher proportion of females in patients with radiological evidence of subchondral cysts. These patients also had a greater varus deformity preoperatively.

Conclusion: With a radiological prevalence of 30.6%, subchondral cysts should not be considered a cardinal radiological feature of osteoarthritis. Subchondral cysts may be associated with the female gender and genu varum.

Keywords: Geodes, osteoarthritis, radiological features, subchondral cysts.

INTRODUCTION

Ageing of the population and increasing obesity contribute to morbidity across the world. Osteoarthritis (OA) is the most prevalent medically treated arthritic condition globally [1, 2]. Obesity has reached epidemic proportions in Asia and as a result, the continent faces a grave burden of obesity-related disorders, of which OA is one [3]. Diagnosis of OA is generally made on the basis of clinical examination and/or radiography. It has been taught generations after generations that there are four cardinal radiological findings of OA. These features are joint space narrowing, presence of osteophytes, subchondral sclerosis and subchondral cysts. However, evidence from two decades ago mentions subchondral cysts as a rare feature that is usually not seen on radiographs [4]. Despite the fact that subchondral cysts are often cited as a common finding in OA, their etiology is still not well understood. In 1940, Freund [5] found evidence that pressure-induced intrusion of synovial fluid may cause enlargement of cystic lesions. More recently, Durr *et al.* [6] proposed that stress-induced microfractures of the subchondral bone may be primary events in the development of subchondral bone cysts in OA. Although subchondral cysts are currently taught as being one of the cardinal features of OA, the authors of this study questioned their radiological prevalence in Asian patients with established

OA of the knee. The purpose of this study is to evaluate the prevalence and epidemiology of subchondral cysts in pre-operative OA knees of Asian patients, in a bid to challenge the notion that presence of subchondral cysts is one of the four cardinal radiological features.

MATERIALS AND METHODOLOGY

From January 2006 to May 2012, all patients who underwent elective total knee arthroplasty for knee OA were retrospectively studied. A diagnosis of OA was made based on a combination of clinical, radiological and arthroscopic methods. Patients from a single surgeon, the senior author of the paper, were selected for consistency of diagnosis. Our Institutional Review Board approved the study.

Exclusion criteria were inadequacy of radiographs, diagnosis other than OA and patients with previous traumatic injury of the knee joint. Based on these exclusion criteria, a total of 78 knees were excluded. The final study group consisted of 806 patients (171 men and 635 women; age range, 50-84 years; average age, 66 years) with OA of the knee joint. Of these 806 knees, 393 (48.8%) were left and 413 (51.2%) were right. The plain radiographs of the knee most recent relative to the date of surgery were selected for review in all patients. Three views were available for all radiographs - the weight-bearing anteroposterior, lateral and skyline views. An independent reviewer used the K&L grading scale (Table 1) to determine the presence of the radiological features of OA in each knee. The images from the original article were used as references [7].

*Address correspondence to this author at the Department of Orthopaedic Surgery, Singapore General Hospital, Outram Road, 169608, Singapore; Tel: (65) 9004-5495; Fax: (65) 6667-8701; E-mail: hamidrazak@gmail.com

Table 1. Kellgren-Lawrence Grading System for Osteoarthritis

Grade	Radiologic Findings
0	No radiological findings of osteoarthritis
I	Doubtful narrowing of joint space and possible osteophytic lipping
II	Definite osteophytes and possible narrowing of joint space
III	Moderate multiple osteophytes, definite narrowing of joint space, small pseudocystic areas with sclerotic walls and possible deformity of bone contour
IV	Large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone contour

The prevalence of each of the four radiological features (narrowed joint space, osteophytes, subchondral sclerosis, subchondral cysts) of OA was then calculated for all the knees. A cross-proportion Z-score was calculated and subsequently P-values were interpreted from the Z-score to evaluate if the differences in proportions were significant. Demographics and preoperative data were compared between patients with and without radiological evidence of subchondral cysts. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) Version 20 (IBM® SPSS Statistics, Armonk, New York, USA).

RESULTS

The prevalence of each radiological feature can be seen in Table 2. Whilst a large proportion of the patients had radiological evidence of narrowed joint space, osteophytes and subchondral sclerosis, only 247 patients showed radiological signs of subchondral cysts. Table 3 shows that the differences observed in the prevalence of all four radiological features were statistically significant.

Table 2. Prevalence of Each Radiological Feature

Radiological Feature	Present (%)	Absent (%)	95% CI of %
Narrowed joint space	802 (99.5)	4 (0.5)	98.6 - 99.8
Osteophytes	791 (98.1)	15 (1.9)	96.9 - 98.9
Subchondral sclerosis	711 (88.2)	95 (11.8)	85.8 - 90.2
Subchondral cysts	247 (30.6)	559 (69.4)	27.6 - 33.9

Table 4 shows the comparative statistics between patients with and without radiological evidence of subchondral cysts. A higher proportion of patients with evidence of subchondral

Table 3. Interpretation of p-Values from Z Score

	Narrowed Joint Space	Osteophytes	Subchondral Sclerosis	Subchondral Cysts
Narrowed joint space		0.0097	< 0.0001	< 0.001
Osteophytes			< 0.0001	< 0.001
Subchondral sclerosis				< 0.0001
Subchondral cysts				

cysts tended to be females with a more pronounced varus deformity.

DISCUSSION

The aim of this study was to evaluate the prevalence of subchondral cysts in pre-operative OA knees of Asian patients, in a bid to challenge the notion that presence of subchondral cysts is one of the four cardinal radiological features and to set the tone for future studies to correlate the clinical implications of subchondral cysts.

Although the focus of this paper is subchondral cysts associated with OA, it should not be forgotten that cystic changes in the bones are also associated with other conditions. Some of these conditions include rheumatoid arthritis [8], calcium pyrophosphate deposition disease [9] and osteonecrosis [10]. Various explanations have been offered with regards to the pathogenesis and location of the cysts in the above-mentioned conditions. In osteoarthritis, subchondral cysts occur on the pressure segment of the femoral head in association with loss of articular space. However in rheumatoid arthritis, they are initially noted at the chondro-osseous junction and subsequently involve the entire femoral head. The cysts appear in the necrotic segment of the femoral head in osteonecrosis while in calcium pyrophosphate deposition disease, they resemble those in osteoarthritis but are larger, more numerous, and more widespread [10].

Simon *et al.* [4] described subchondral cysts as being typically small, well-defined and located adjacent to the medial tibial cortex with their long axes in the sagittal plane. He added that they usually present no diagnostic difficulty. Cysts in osteoarthritic joints are usually viewed as a radiolucent osteolytic lesion with a sclerotic border beneath the articular cartilage. However, if based on the strictest definition of a cyst being a closed cavity lined by epithelial cells containing liquid or semisolid material, then these radiolucent lesions seen plain radiographs of an osteoarthritic knee should not be considered cysts because subchondral cysts are not surrounded by such a lining [11-14]. Thus, there have been other terms such as "geodes" used to describe subchondral cysts [10].

It is widely agreed that the pathogenesis of subchondral cysts remains obscure and uncertain [11]. There have been a number of theories postulated on the pathogenesis. The two main postulated theories are the synovial intrusion theory and the bony contusion theory. Freund [5] suggested that it could be secondary to pathology of the synovium extending into the bone due to the similarity of synovial fluid to the cystic fluid, abnormal articular cartilage over the cyst and displaced pieces of surface cartilage within the cyst. This is

Table 4. Comparative Data

Characteristics	Group 1	Group 2	P-Value
	Patients with Radiological Evidence of Subchondral Cysts (n=247)	Patients with No Radiological Evidence of Subchondral Cysts (n=559)	
Demographics			
Mean Age (range) (years)	66 (48-83)	66 (32-85)	1.00
Gender: Female (%)	84	76	0.009
Percentage of Males with Subchondral Cysts (%)	23		0.007
Percentage of Females with Subchondral Cysts (%)	33		
Mean Body Mass Index (range) (kg/m ²)	28.6 (19.8-45.0)	28.1 (18.9-46.4)	0.165
Operated Limb: Right (%)	55.1	49.6	0.149
Race			
Chinese (%)	88.2	87.7	0.840
Malay (%)	6.9	6.4	0.795
Indian (%)	4.9	5.9	0.556
Pre-operative Measurements & Scores			
Alignment (s.d.) (degrees)*	6 (±8)	4 (±8)	0.001
Genu Varus (%)	80.2	73.7	0.039
Knee Society Score (s.d.)	37 (±8)	36 (±8)	0.102

*Positive value indicates varus.

supported by the presence of a communication between joint cavities and the subchondral cyst. However, a communication is not observed all the time. The bone contusion theory seems to explain the absence of a communication. The bony contusion theory postulated by Rhaney and Lamb [15] suggests that impact between opposing surfaces of bone, which have lost its protective cartilage results in microfractures and bone necrosis. Synovial fluid intrudes the bone when the bone attempts to heal by osteoclastic resorption of the necrotic bone. This is supported by the lack of communication between the joint cavity and the subchondral cyst, presence of metaplastic cartilage and osteoclasts in the disrupted bone.

Even the correlation of subchondral cysts with clinical presentation is not clear. Most textbooks state that subchondral cysts are usually asymptomatic [13, 14]. Fritz [16] in 1979 reported that the subchondral cysts remain asymptomatic for years. Very occasionally, the ganglion of the underlying bone may exert pressure on the soft tissue causing it to swell, causing some pain. Otherwise, he reports that most of these cysts are clinically silent and are incidental finding when radiographs are taken for other reasons.

We did not find any literature reporting on the epidemiology of subchondral cysts. The results of our study show a significantly higher proportion of females in patients with radiological evidence of subchondral cysts. We do know that OA is more common in women after menopause [17]. Bay-Jensen *et al.* [17] in his review article explains that hypoestrogenaemia in menopause seems to augment OA progression, although estrogen does not block articular cartilage degradation. Estrogen receptors are present in most if not all tissues, suggesting that the pleiotropic actions of

estrogen on cartilage and all other tissues may be important in the progression of OA. We postulate that the loss of articular cartilage augmented by hypoestrogenaemia may be a precursor to the formation of subchondral cysts by the pathogenesis suggested by Rhaney and Lamb [15]. Females are also known to have higher body percentage of fat than males. Leptin is secreted by adipocytes and regulates body weight through its effects on food intake and energy expenditure [18]. Leptin is a major regulator of bone remodeling that acts on osteoblasts, therefore preventing osteoporosis [19] but increasing the risk of OA by affecting subchondral bone morphology [20]. This could be the molecular basis for subchondral cyst formation in females.

Our results also show that there is a significantly higher proportion of genu varum deformity in patients with radiological evidence of subchondral cysts. It is well known that medial joint wear is more common in OA of the knees [21]. This differential wear causes the commonly seen genu varum deformity seen in OA of the knees, which in turn causes an imbalance in the condylar forces with greater contact forces in the medial aspect of the knee joint [22]. This may support the pressure-induced intrusion theory for formation of subchondral cysts suggested by Freund [5].

Subchondral cysts have been “traditionally” taught to be one of the four cardinal radiological features of osteoarthritis. However based on our results, subchondral cysts are only radiologically present in 30.6% of the knees we reviewed. Whereas, the other key features are present in close to 100% of the knees for narrowed joint space (99.5%) and osteophytes formation (98.1%). The third most prevalent feature, subchondral sclerosis is present in close to 90% of the knees. Unfortunately, there are no other studies of a

similar nature for comparison of our results. Should subchondral cysts still be considered a cardinal radiological feature of osteoarthritis and be taught as one? The authors believe not. However, the clinical relevance of detecting subchondral cysts radiologically is not well studied. Through this study, we hope to follow-up on correlation of subchondral cysts with intra-operative findings and management as well as post-operative pain. We found one study to date by Torres *et al.* which concluded that relationship with pain severity was of borderline significance for bone cysts [23]. Interestingly, our study suggests that subchondral cysts may be associated with the female gender and a more pronounced genu varum deformity.

The strengths of our study include a relatively large sample size with consistency of diagnosis as all patients belonged to a single surgeon. Inter-observer bias is not an issue in our study as all plain radiographs were evaluated by a single reviewer based on a standard atlas. Our study is probably the first one studying the epidemiology of subchondral cysts in patients with knee OA. However, the results of this study must be interpreted in context of its limitations. The major limitation of this study stems from its retrospective nature. Effects of confounders are inevitable especially in a retrospective study. Furthermore, causality cannot be implied as this is an observational study. Surgeon bias in patient selection invariably has its effect on our data too. In addition to these, there is likely to be sample bias due to a high proportion of females in our study group. This is likely due to the epidemiology of OA in our region. Our results also lack generalizability as we only included the knee joint and our patients are ethnically Asian. We also did not report functional outcomes of these patients due to a paucity of prospective data for a majority of these patients. However, we still believe that this study will promote future prospective studies evaluating the clinical impact of subchondral cysts.

CONCLUSION

Subchondral cysts may be a late feature of OA of the knee as part of the pathological basis for disease. However, based on its low prevalence as seen from our study, we believe that it should not be considered a cardinal radiological feature of knee OA. Subchondral cysts may be associated with the female gender and a more pronounced genu varum deformity. The way ahead will be to explore if presence or absence of subchondral cysts has any impact on surgical management and clinical outcomes of patients with knee OA.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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